Peri-implant bone density around implants of different lengths: A 3-year follow-up of a randomized clinical trial

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Abstract: OBJECTIVES Short dental implants are frequently placed, however, little is known about the effect of the loading force regarding an enhanced crown-to-implant ratio. The aim of this study was therefore to assess bone density changes after a 3-year period, on radiographs acquired from a randomized, controlled two-centre clinical study comparing implants of 6 and 10 mm of length. MATERIALS AND METHODS Three predefined areas were chosen on standardized X-rays in order to assess grey-scale values of the peri-implant bone: One at the tip of the apex and two at half-length on the mesial and distal sides of the implant. Radiographs at all follow-up appointments had previously been calibrated using control fields in areas of constant density. RESULTS Around short implants, peri-implant bone displayed significantly higher differences in grey-scale values (p = .031) after 3 years, indicating a higher degree of mineralization. This phenomenon was not observed around long implants. CONCLUSIONS A higher degree of mineralization around short implants was recorded. Whether this finding goes along with hampered bone adaptability, and accordingly, higher failure rates of short implants must be studied further in long-term clinical trials.

DOI: https://doi.org/10.1111/jcpe.12737

Peri-implant Bone Density around Implants of Different Lengths: A 3-year Follow-up of a Randomized Clinical Trial

Running Head: Peri-implant bone density

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Keywords: dental implants, RCT, bone level, dental radiography

Conflict of Interest and Source of Funding Statement
The authors declare that they have no financial or other relationships that might lead to a conflict of interest. The authors have stated explicitly that there are no conflicts of interest in connection with this article. This study was supported – in part - by a grant of the International Team for Implantology, Basel, Switzerland (ITI Nr 517-2007).

Abstract:

Objectives: Short dental implants are frequently placed, however, little is known about the effect of the loading force regarding an enhanced crown-to-implant ratio. The aim of this study was therefore to assess bone density changes after a three-year period, on radiographs acquired from a randomized controlled two-center clinical study comparing implants of 6 and 10 mm of length. **Materials and Methods:** Three predefined areas were chosen on standardized X-rays in order to assess grey-scale values of the peri-implant bone: One at the tip of the apex and two at half-length on the mesial and distal sides of the implant. Radiographs at all follow-up appointments had previously been calibrated using control fields in areas of constant density. **Results:** Around short implants, peri-implant bone displayed significantly higher differences in grey-scale values (p=0.031) after three years, indicating a higher degree of mineralization. This phenomenon was not observed around long implants. **Conclusions:** A higher degree of mineralization around short implants was recorded. Whether this finding goes along with hampered bone adaptability, and accordingly, higher failure rates of short implants must be studied further in long-term clinical trials.

Clinical Relevance

Scientific Rationale for the study:

Data from clinical trials still do not provide data about factors potentially leading to implant failure on the long term caused by functional or relatively excessive load due to a smaller bone-implant interface in shorter implants.

Principle findings:

Peri-implant bone around 6mm test implants showed a significant higher degree of mineralization after a 3-year observation period as compared to control implants of 10mm length.

Practical implications:

Though stronger corticalization provides the advantage of enhanced implant stability, biological adaptation to functional or inflammatory challenges might be impeded.

Introduction

Recent systematic reviews confirm high implant survival rates of 94-95% after more than ten years of loading (Moraschini et al. 2015, Albrektsson and Donos 2012) and satisfying success rates of 84-90% (Albrektsson et al. 1986, Clementini et al. 2012) depending on the applied success criteria and the follow-up periods investigated. Nevertheless, implant reconstructions are not free from technical and biological complications, which were reported in 16% and 7% of the cases after 5 years of loading, respectively (Jung et al. 2012).

Among the biological problems, peri-implantitis represents a well-known complication and the most common reason for failure (, respe. 2012). If left untreated, peri-implantitis may ultimately result in implant loss. Worthy of note is that it is not the only reason for biological implant failure. For instance, there is an ongoing scientific discussion about a possible impairing influence of increased loading forces or – with other words – increased crown-to-implant ratio (CIR) on the bone-implant interface and therefore a possible negative influence on implant survival (Mezzomo et al. 2014, Quaranta et al. 2014, Chang et al. 2013). The clinical impression of an ongoing adaption process within the peri-implant bone structure after implant placement (Mangano et al. 2015) is supported by numerous finite element studies (Rungsiyakull et al. 2011, Lee and Lim 2013, Akca et al. 2010), animal models (Halldin et al. 2014) and histologic analysis of retrieved implants from man (Coelho et al. 2009).

Radiographically, an optically denser peri-implant bone may appear after a certain time of loading. This enhanced mineralization process, which coincides along with an increased histologic bone-to-implant contact (BIC), might be understood as an adaption due to the loading forces which strengthen the mechanical stability of the implant in man (Hasan et al. 2015). Highly mineralized bone, however, also implies a reduced biological response, with potential disadvantages regarding bone turn-over and functional adjustment (Chvartszaid et al. 2008, Simons et al. 2015) and a downgraded vascularization (Chanavaz 1995, Eiseman et al. 2005)

On very rare occasions with short 6 mm implants, implant loosening was noticed even several years after asymptomatic loading. These implants had not shown clinical signs of inflammation such as bleeding-on-probing. Likewise, no increase in peri-implant pocketing, no suppuration nor marginal bone loss were found, which would have all been typical indications of peri-implantitis.

However, in these cases the peri-implant bone appeared clearly denser on the radiographs than at the moment of initial loading. Furthermore, a distinct radio translucent gap was visible around some of these implants, reflecting a complete loss of bone-to-implant contact.
Therefore, the aim of this study was to retrospectively assess the density of peri-implant bone around short and long implants placed during a two-center RCT study after 3 years. Our hypothesis was, that we would find an increased radiographic density around short (6 mm) implants as compared to longer (10 mm) control implants.

Materials & Methods

The present study was performed as a sub-analysis of a previous RCT that had focussed on the clinical outcomes of implants of two different lengths (Sahrmann et al. 2016). Radiographs were taken as part of a two-center randomized prospective trial which aimed to compare the clinical outcome of implants of two different lengths in replacing single teeth in the posterior jaw (German Clinical Trials Registry DRKS00006290). This trial had been approved by the local ethical committee (StV Nr. 07/13; Sahrmann et al. 2016).
In brief, SLActive® standard plus implants (Straumann, Basel, Switzerland) of either 6 mm (test group) or 10 mm (control group) length were placed in healthy patients with missing single teeth in the lateral upper or lower jaw. Implantation was performed according to the manufacturer's instructions and following a computerized randomization list.
No bone augmentation was performed. Heavy smokers (>19 cigarettes/d) were excluded from study participation. After 10 weeks, the implants were loaded with screw-retained porcelain fused to metal crowns. Immediately afterward, individual X-ray splints using a parallel technique were prepared and radiographs were taken during the same appointment (baseline). After one, two and three years, during regular follow-up maintenance appointments, when oral hygiene reinstruction and tooth polishing were performed, standardized X-rays of the implants were taken again using the same individualized splints to ensure standardized images. More detailed information is provided in the publication of the clinical results after 3 years of loading (Sahrmann et al. 2016).

X-ray assessment

For all radiographs Digora Soredex plates (Soredex, Tuusula, Finland), size 2 had been used. Radiographs were taken (Heliodent plus, Sirona, Bensheim, Germany) at a voltage of 70 kV and a explosion time of 0.1 ms for upper molars, 0.08 ms for upper premolars and lower molars and 0.05 ms for lower premolarsand a tube length of 10 cm. The distance between tube and plate of 5.5 cm was defined by the plate holder system. On each radiograph, five standardized assessment areas of interest (AOI; 18x18 pixel) were marked. Two test areas c_1 and c_2 were placed at half-length of the intraosseous part of the implant, one in the mesial and one on the distal peri-implant bone right next to the implant surface. A third AOI was placed on the peri-implant bone right next the tip of the apex. Furthermore, for calibration purposes, two control areas were placed into either metal or composite restorations or dentin areas, which presumably would not change density during the years of observation (Fig. 1). The position of the AOI - together with the implant location - were defined on an inalterable computerized mask on the baseline radiograph. This mask was copied and superimposed on the follow-up radiography. In case of optical distortions, this mask was adapted in its vertical or horizontal dimension in order to avoid any inaccuracies.

The analysis of the grey scale value of the AOI was performed with ImageJ (Vs. 1.46r, National Institutes of Health, USA). Initially, the baseline grey scale values for all implants were assessed calculating the "mean" grey scale following *Analyze>measure* command in ImmageJ. On each of the follow-up images, the grey scale values of both control areas were taken and their mean value was calculated. By dividing this follow-up value by the baseline mean value a calibration factor (CF) was obtained. The latter was used to correct for any possible change of the ground brightness of these pictures. Therefore, each grey scale value of the respective AOI was divided by this calibration factor.

Finally, difference of the grey scale value (Δ GSV) of each area of interest (t_{1-3}) was calculated by substracting the baseline GSV from the calibrated GSV obtained at the respective time point.

Statistics

Data for grey shade values and the differences over time were checked for normal distribution using the Shapiro-Wilk and Kolmogorow-Smirnow test. If both tests indicated a normal distribution, results were tested for intragroup differences (longitudinal changes) with the paired student's t-test, and intergroup differences with unpaired student t-tests. If the distributions were not normal the Wilcoxon Signed Rank Test was used to test for intragroup differences (longitudinal changes) and the Mann-Whitney U-test to test for intergroup differences. Baseline dichotomous data was tested for possible differences by the Pearson's chi-square test. A random effect model (SPSS MIXED procedure with REPEATED statement) was performed in order to investigate the effect of implant lengths, crown-to-implant ratio, gender, smoking status, history of periodontitis and investigation period on the differences of the grey scale values (ΔGSV) over the period of three years. The mean of all test areas was used as response variable.

For all performed tests a level of significance of 5% was set.

Results

For the present study, follow-up X-rays of 87 implants (39 control and 48 test) could be assessed.

Baseline data for test and control implants did not show any differences regarding age, gender, localization of the inserted implant in the jaw, smoking or history of periodontitis. Likewise, the data for PlI, BOP, PPD and BL showed no significant differences (Table 1).

Assessing the change of the grey scale values over time, there was a significant change for the test areas of the short implants: The peri-implant bone areas appeared brighter with time or – in other words – the grey-scale difference was higher. No such effect could be observed for the control implants of 10 mm length (Table 2).

Accordingly, there was a significant difference between the change of grey-scale values over time between the groups: while the peri-implant bone around short implants showed no enhanced difference in optical density after 1y of loading (p=0.117) as compared to the controls, the difference between the groups turned out to be significant after 2 and 3 years of loading (p=0.017 and 0.031, respectively), indicating a more pronounced mineralization around the test implants (Fig. 2 and 3) over time.

Testing for possible effects only the implant length (p = 0.008) for the mean of all the test areas) had an effect. Accordingly, neither crown-implant-ratio nor patient's gender, smoking habits or history of periodontitis showed any statistically significant effect. The effect of investigation time on the ΔGSV was found not be significantly different between the groups, i.e. no interaction effect was found between implant length and investigation time. In both groups, the most pronounced change in ΔGSV was between first and second year of loading (p = 0.004).

Discussion

With the advantage of offering less invasive treatment, short implants are currently enjoying great popularity, even though high-level clinical studies are still rare. Especially the issue of a possible negative influence of an enhanced crown-to-implant ratio on the biological interface of bone and implant is still a matter of unresolved discussion. Clinical data and basic research regarding this issue are still scarce. Therefore, radiographs from a RCT comparing short and longer implants were compared in order to assess the peri-implant bone density around implants of different lengths three years after loading.

Over the study period examined, a significant increase in grey-scale values of the peri-implant bone around short implants was observed, but not around the longer control implants. Accordingly, from the second year of loading onwards the grey scale value change was more pronounced around the short implants. Therefore, our hypothesis was confirmed.

On conventional radiographs, brightening of bone structure in the radiographs indicates a higher degree of mineralization (Meunier and Boivin 1997). A denser peri-implant bone may constitute to a higher mechanical stability and an enhanced bone-to-implant contact (BIC; Abrahamsson et al. 2009).

Generally, bone morphology in terms of form and structure is not static but constitutes a dynamic equilibrium subjected to continuous changes around a loaded implant. This change is characterized by a high turnover rate of the bone structure, which allows prevention of chronic damage and adaptation to external stimuli (McCauley and Nohutcu 2002, Coelho et al. 2009). Loading forces, which are transferred via dental implants, are such stimuli for the alveolar bone and trigger its functional adaptation (Heinemann et al. 2015). Therefore, even after initial osseointegration of the implants, the structural changes continue for a prolonged time of remodeling (Hadjidakis and Androulakis 2006). Bone remodeling occurs as a response to the exposure to both functional loading on one hand and oral habits like clenching or pressing on the other hand. This process is based on the translation of mechanical stimuli by osteocytes, which organize an equilibrated homeostasis of the bone household by regulation of blood calcium level and induction of osteoblast and osteoclast function (Burger et al. 1995, Sims and Gooi 2008). Accordingly, it has been shown in experimental studies, how bone remodeling can be influenced: Rungsiyakull and co-workers showed in a finite element model, that if the dynamic load on the implants is changed by different angulation of the crowns' cusps, the peri-implant bone density will be enhanced (Rungsiyakull et al. 2011). Piccini et al. showed in a rat model, that the application of high forces on implants lead to a radiologically denser peri-implant bone. Coincidentally, implant stability enhanced (Piccinini et al. 2016). This ongoing adaptation of the peri-implant bone structure and its interaction with the implant surface has been defined as tertiary implant stability (Hasan et al. 2015). It has been interpreted as a physiological adaptation to higher loads, since a higher degree of mineralization comes along with an enhanced mechanical stability (Bergkvist et al. 2010). Improving the implant's mechanical stability by enhancing the degree of mineralization, however, results in a concurrent loss of biologic capability of the bony tissue. During this change, spongeous bone gets transferred into cortiical structures (Abrahamsson et al. 2004). Spongeous bone marrow chambers however are rich of blood vessels, mesenchymal cells like osteoprogenitor cells and cytokines (Abrahamsson et al. 2004). Cytokines in turn are responsible for the bone's capacity of reparing damaged osseous tissue and forming new bone structure (Friedenstein et al. 1968, Long 2001). Accordingly, with rising degree of mineralization the bone's biological response is supposed to get hampered. In fact, during the three-year investigation period of the present study one of the short implants was indeed lost without any clinical symptoms of inflammation (Sahrmann et al. 2016), but with an obviously pronounced corticalization of the peri-implant bone. For this implant, only a slight marginal bone loss was observed on the radiograph but corticalization and the absence of bleeding on probing and deepened probing depths contradicted an inflammatory etiology (Fig. 4). The affected implant became mobile without evidence of critical marginal bone loss on the radiograph or any noticeable bone loss on the buccal side or in the depths of the implant bed. The implant got mobile and could easily be removed. A new implant of normal length was placed at the same site without bone augmentation. This second implant has been successfully loaded for another 4 years now without any symptoms.

During the year 3-6 of the ongoing study, we experienced the loss of three more short implants with the same symptoms of non-inflammatory loosening, whereas no implant was lost from the control group.

Despite the possible impact of the implant length itself on the degree of mineralization of the peri-implant bone, we failed to detect an effect of the crown-to-implant ratio in the regression analysis. This somehow contradicting result may be attributed to the – statistically spoken – small study size and due to confounding factors (Wang et al. 2015). On one hand these might be patient-related issues such as smoking (Moheng and Feryn 2005) or clenching (Manfredini et al. 2011) and prosthetic-related issues on the other hand, such as the exact height of the restorations and correspondingly static and dynamic loading forces (Chang et al. 2013)). The finding that the crown-to-implant ratio had no effect on the radio-opacity of the neighboring bone, however, is in accordance with several recent publications of finite element and clinical trials (Birdi et al. 2010, Bulaqi et al. 2015, Mangano et al. 2016) that failed to show any impact of CIR on the peri-implant bone.

An important limitation of the present study is that the results are based on a conventional radiographic assessment. In fact, an evaluation of the exact nature of the bone quality and the bone quantity, in terms of the bone-to-implant contact, would require a more invasive approach like histomorphometric analysis based on biopsies (Sağirkaya et al. 2013). Such biopsies, however, are for obvious reasons impossible in the context of such a clinical study, especially within a longitudinal design. In addition, the present results are based on a two-dimensional assessment from conventional radiographs only. Therefore, bone density was – apart from the apical assessment - considered only from the mesial and distal aspect. However, we gained no information about the circumferential situation or at least the buccal and oral sites. Three-dimensional cone beam computerized tomography assessment might have provided a more detailed data set (Shakibaie-M 2013), even if artifacts closed to titanium implants render an exact assessment difficult or even impossible (Ritter et al. 2014).
Follow-up radiographs had been calibrated to the baseline picture before GSC values were compared. By using the mean of the calibration factors from two calibration areas we tried to minimize possible inaccuracies. Still, the question whether dentine areas itself or even metal or composite reconstructions might gradually change their radio-opacity is still unclear and to the best of the authors' knowledge has not been assessed yet. The present study, however, was conducted with the aim to assess for the first time whether a pronounced mineralization of the peri-implant bone around short implants is a true fact with a potentially clinical impact. Nevertheless, additional and more sophisticated investigations based on long-term observational studies will have to assess both the exact histological and three-dimensional nature of the bone change around short implants and consider its effect on implant survival and success.

Table 1 Baseline patient characteristics.

	Short implants	Control implants	p-value
Male/female	20/19	21/27	0.523
Smokers	11	12	0.809
History of periodontitis	23	22	0.282
Localisation			
Upper M	3	9	
Upper PM	8	15	
Lower M	17	18	
Lower PM	11	6	0.124

M – Molars PM – Premolars
Differences were tested with Pearson's Chi-square test

Table 2 Mean values of ΔGSV (± standard deviation) for the individual areas of interest ($t_{1\text{-}3}$) and the mean value of the latter t_{ges} at different time points (1-3 years). Bold p-values indicate significant intra-group difference of GSV between baseline and the respective time point (Mann-Whitney-u test, level of significance = 0.05).

	Arbitrary Units (mean ± std)	p-value
Short implants		
1 year		
t_1	10.3 ± 14.0	**0.002**
t_2	13.8 ± 23.7	**0.002**
t_3	7.7 ± 12.0	**0.008**
t_{ges}	10.6 ± 15.6	**0.001**
2 years		
t_1	4.5 ± 12.6	**0.036**
t_2	4.3 ± 10.7	**0.018**
t_3	4.3 ± 13.1	**0.032**
t_{ges}	4.1 ± 9.3	**0.011**
3 years		
t_1	6.0 ± 13.3	**0.028**
t_2	4.3 ± 13.1	**0.049**
t_3	4.4 ± 10.3	**0.018**
t_{ges}	4.9 ± 11.6	**0.019**
Control implants		
1 year		
t_1	-1.0 ± 15.3	0.488
t_2	3.5 ± 16.8	0.179
t_3	3.0 ± 13.9	0.122
t_{ges}	2.1 ± 13.4	0.153
2 years		
t_1	-2.9 ± 14.5	0.104
t_2	1.7 ± 17.6	0.281
t_3	-2.7 ± 16.4	0.269
t_{ges}	-1.3 ± 13.8	0.116
3 years		
t_1	-1.3 ± 16.5	0.356
t_2	-4.3 ± 19.3	0.088
t_3	0.9 ± 17.1	0.620
t_{ges}	-1.6 ± 15.5	0.213

Fig. 1 Test and control areas set on the baseline radiograph (A) and the follow up radiographs after 1, 2 and 3 years (B).

$t_{1\text{-}3}$ – test areas in peri-implant bone
$c_{1\text{-}2}$ – control areas for calibration

Fig. 2 Difference of the mean Grey Scale Values (ΔGSV for t_{ges}) for short and control implants at 1, 2 and 3 years after baseline.
The difference of the grey scale values (Δ GSV) was calculated by substracting the baseline GSV from the GSV obtained at the respective time point.

Fig. 3 Grey Scale Values (GSV) for short and control implants at baseline and after 1, 2 and 3 years.

Fig. 4 Implant lost due to mobility after 3 years of loading. The implant did not show clinical symptoms of inflammation besides slight mucositis at chinging sites. Peri-implant bone appears markedly denser around the implant.

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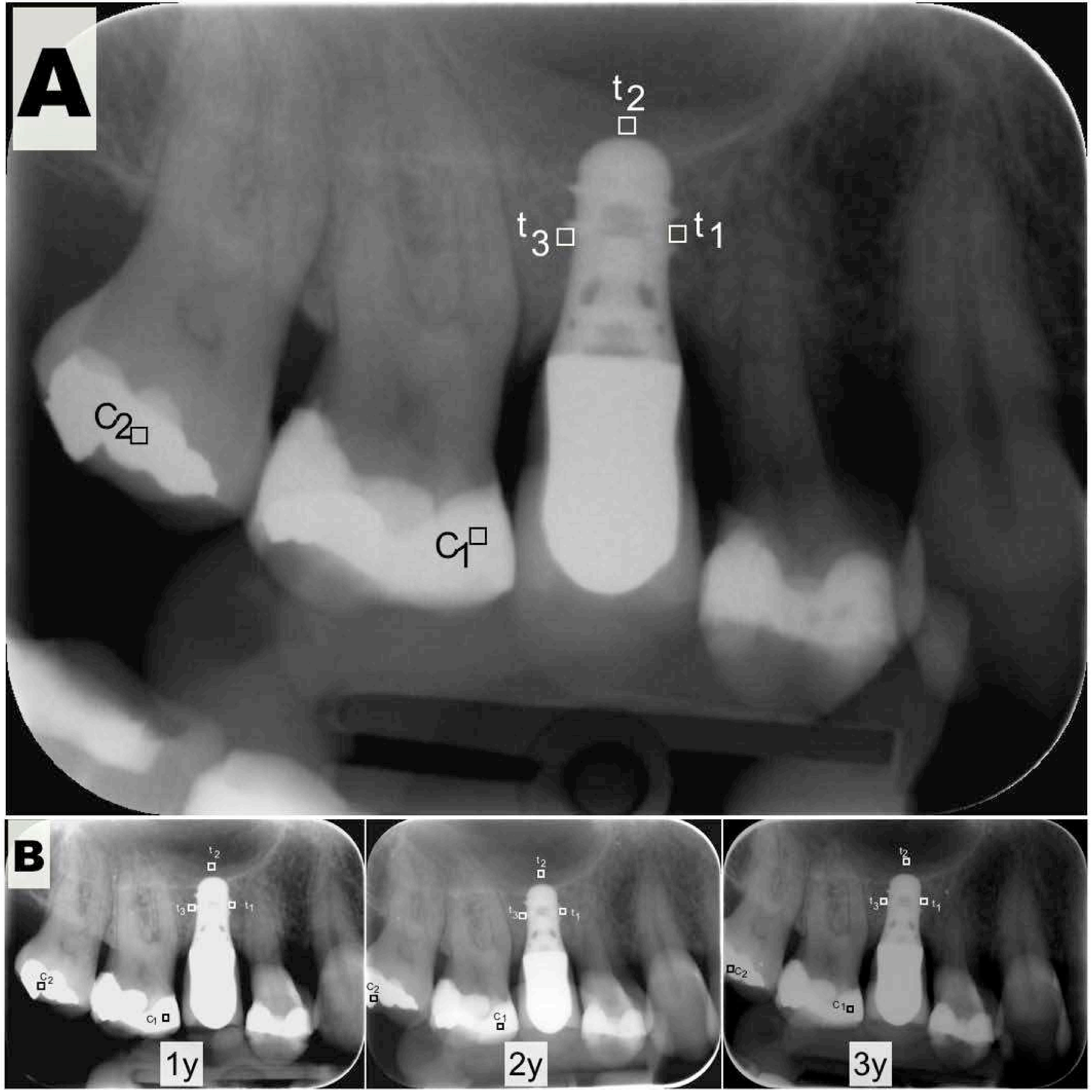
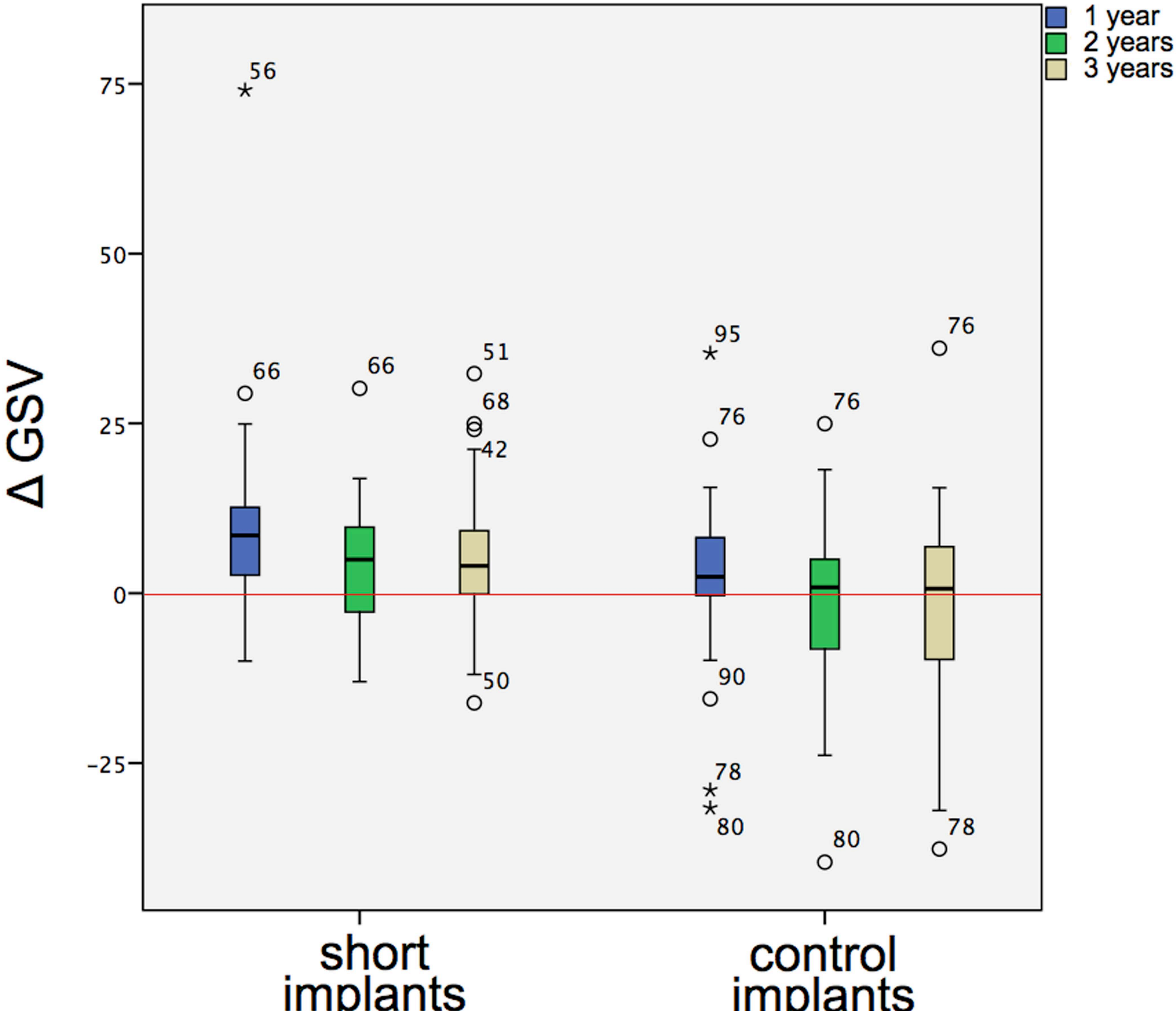

A
t2
t3
t1
C2
C1
B
1y
2y
3y



1 year
2 years
3 years
75
50
25
0
-25
Δ GSV
56
66
66
51
68
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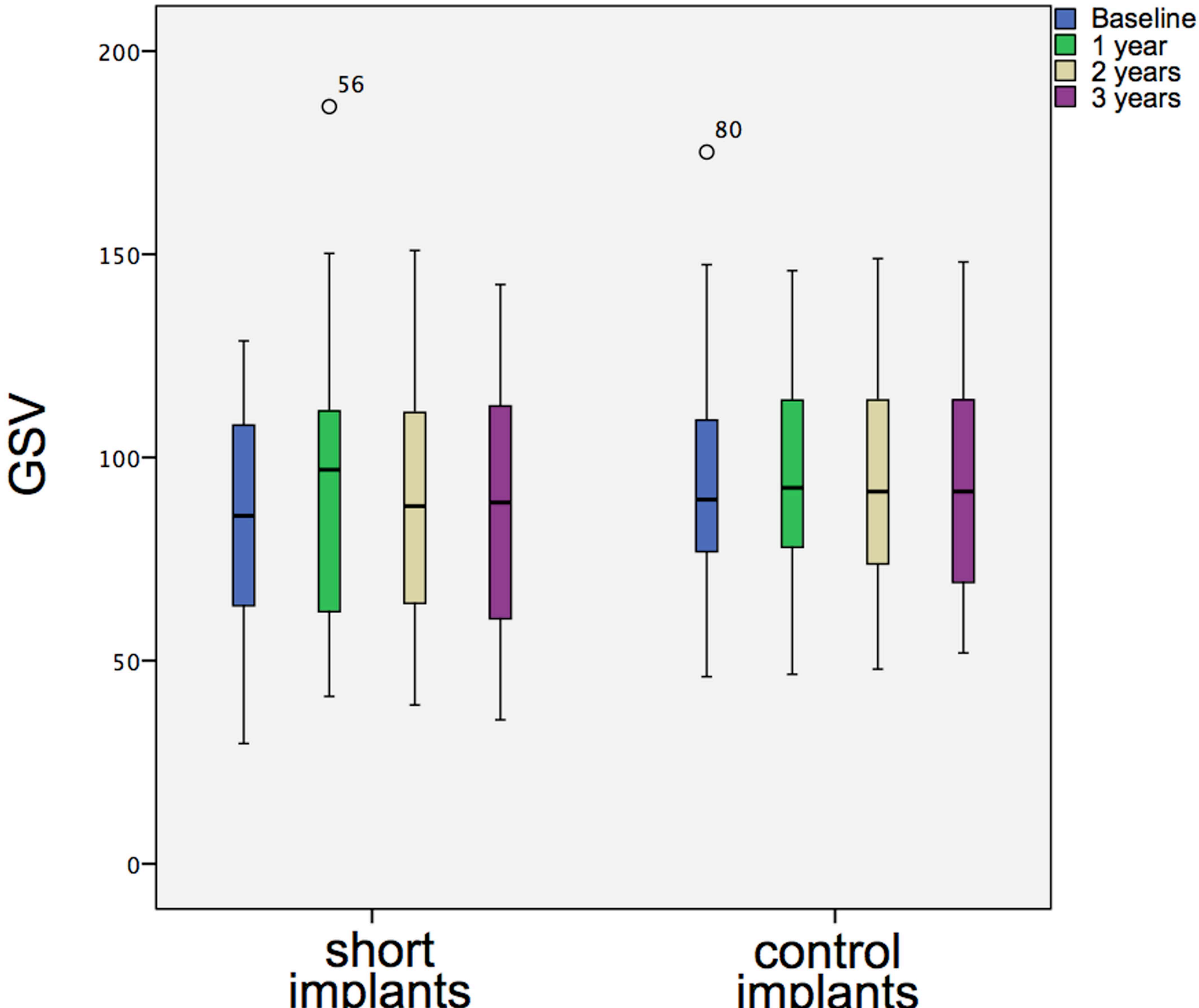
95
76
90
78
80
76
80
76
78
short implants
control implants


GSV
200
150
100
50
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56
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short implants
control implants
Baseline
1 year
2 years
3 years